DECLARATION OF DR. MARTHA KAREN NEWELL

I, Martha Karen Newell, Ph.D., declare as follows:

1. I make this declaration in support of U.S. Serial No. 09/599,760 on which I am named as the sole inventor.

2. I am a Professor of Immunology at the University of Colorado in Colorado Springs. I have been performing research on uncoupling protein (UCP) expression since 1998. Prior to that time, I performed research in the field of immunology generally and, more specifically, to examine the mechanisms in MHC class II signaling and apoptosis and MHC class II mediated signaling and autoimmune disease.

Cancelled 4/19/03 JZ

3. I have performed several experiments in my laboratory which relate to my discovery of UCP in lysosomes, including examining the relationship between lysosomal pH and UCP inhibitors and activators.

4. A recent article by Arsenijevic *et al.* suggests that a decrease in lysosomal UCP is useful for preventing and treating infections. In the article, a relationship between uncoupling protein-2 (UCP2) expression and both the limitation of reactive oxygen species (ROS) and macrophage-mediated immunity is described (see Exhibit 1, Arsenijevic *et al.*, Disruption of the uncoupling protein-2 gene in mice reveals a role in immunity and reactive oxygen species production, *Nature Genetics*, 2000, 26(4):387-8. Applicant has cited this reference in an IDS dated May 15, 2001.). Arsenijevic *et al.* found that compared to wildtype mice, $UCP2^{-/-}$ (knockout) mice resisted and eliminated infectious challenge more efficiently. They believe the macrophages of the knockout mice have a greater capacity to generate ROS, which is consistent with observations of decreased UCP2 mRNA concentrations associated with increased ROS and

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increased UCP2 mRNA concentrations associated with decreased ROS. Accordingly, the Arsenijevic *et al.* data demonstrate that decreasing UCP function (by eliminating the UCP2 gene) is useful to prevent or treat infection. Arsenijevic *et al.* did not recognize that UCP was expressed in the lysosome. Based, however, on the finding of the invention that UCP is expressed in the lysosome, the teachings of Arsenijevic *et al.* can be interpreted to mean that loss of lysosomal UCP expression is associated with the ability to treat or prevent infection. Therefore, it is Applicant's assertion that the regulation of lysosomal pH would be useful to treat or prevent infectious disease.

5. I, Martha Karen Newell, Ph.D, declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under §1001 of Title 18 of the United States Code, and that such willful, false statements may jeopardize the validity of this document and any patent which may issue from the above-identified patent application.

January 14, 2002

DATE

Martha Karen Newell

MARTHA KAREN NEWELL, Ph.D